Remarks

Claims 28, 29, and 49 are currently pending in the subject application. By this amendment claims 28 and 49 have been amended. Therefore, claims 28, 29, and 49 remain before the Examiner for consideration. Favorable consideration of the claims as now presented is earnestly solicited.

The amendment of the claims has been done solely for the purpose of lending greater clarity to the claims and for expediting prosecution. These amendments should not be taken to indicate the applicants' agreement with, or acquiescence in, the rejections of record.

The specification has been amended to include a Cross-Reference to Related Application Section.

The subject invention pertains to the unique and advantageous use of Target Binding Assemblies (TBAs) to selectively bind a target binding region (TBR). Advantageously, the TBA's can target an individual control region and not interfere with other cellular sites.

Claims 28, 29 and 49 have been rejected under 35 U.S.C. §112, second paragraph, as being indefinite. In one aspect of this rejection, the Examiner specifically points to the wording of claim 49 as it relates to the components of the TBAs. By this Amendment, claim 49 has been amended to address the Examiner's concerns. Specifically, claim 49 has been amended to clarify that each TBA comprises a DNA recognition unit. Also, reference to "expressed" has been removed. The applicants believe that these amendments address the 35 U.S.C. §112, second paragraph rejections as they relate to claim 49.

In a further aspect of the rejection under 35 U.S.C. §112, second paragraph, the examiner states that "it is unclear whether TBAs are required to bind only to PNA-TNA hybrids or whether TBAs also may recognize and bind single stranded forms of nucleic acid." Without conceding that the TBAs could not be used to bind single stranded polynucleotides, in order to clarify the current claims, claim 28 has been amended to specifically refer to double stranded polynucleotides.

In view of the amendments to the claims, the applicants respectfully request reconsideration and withdrawal of the rejections under 35 U.S.C. §112, second paragraph.

Claim 28 has been rejected under 35 U.S.C. §102(e) as being anticipated by either of Roth *et al.* (U.S. Patent No. 6,017,524) or Gruber *et al.* (U.S. Patent No. 5,830,458). The applicants respectfully traverse these grounds for rejection because the cited references do not disclose or suggest the highly selective and specific methods claimed by the current applicants.

As noted by the examiner, the Roth patent teaches the abatement of translation by binding of antisense RNA to its complement. The Office Action equates the TBA of the instant invention to this antisense RNA binding. However, the TBA of the instant invention and the antisense binding of the Roth patent are distinguishable. The unique ability of the TBAs of the current invention to specifically bind with target double stranded polynucleotides is not disclosed or suggested by Roth *et al.* Advantageously, the design of a TBA allows for a target to be selected that includes identical binding regions found elsewhere in the target sample. Roth's RNA introns are targeted for added specificity; these targeted introns must be "sufficiently different from an intron region of another gene such that no cross hybridization occurs."

The use of the TBAs of the instant invention is similarly distinguishable from the teachings of Gruber *et al.* The highly specific nature of the TBAs of the subject invention is described at, for example, item 6 on page 27 of the applicants' specification. A fundamental feature of the TBAs of the instant invention is the necessity of a high degree of region-specificity: "The TBA must bind the TBR(s) in a fashion that is highly specific to the TBR(s) of interest. That is, the TBA must discriminate between TBRs present in the TNA-PNA hybrid and similar duplex sequences formed by [closely related] hybrids." The Gruber patent does not teach constructs having such a high degree of specificity. In contrast, the instant invention relies on such specificity as described in item 6, page 27, of the specification.

Gruber describes using recombinant retroviruses to introduce a vector construct to interfere with expression of a pathogenic state, but does not teach how these vector constructs interfere. Gruber does not teach how to selectively target binding regions. For example, a vector construct that binds the HIV-LTR will not be a successful therapeutic if it binds NFKB-binding sites in the genome (e.g., the beta2-micro-globulinpromoter, the kappa-light chain promoter, etc.). Thus, the TBAs of

the subject invention are not only different from the Gruber *et al.* construct, but they are also highly advantageous.

For the foregoing reasons, the applicants respectfully request reconsideration and withdrawal of the rejections based upon 35 U.S.C. 102 (e).

Claim 28 has been rejected under 35 U.S.C. §103(a) as being unpatentable over Frankel *et al.* (U.S. Patent No. 5,674,980). The applicants respectfully traverse this grounds for rejection.

First, as has been previously discussed, the instant invention is dependent upon a high degree of region-specificity. Nowhere in the Frankel patent, either expressly or implicitly, is such specificity taught.

Frankel describes the delivery of polypeptides and nucleic acids. In one example a fusion protein of tat and E2 was expressed from delivered genes. Frankel *et al.* do not teach how to selectively target binding regions. The Frankel *et al.* molecule would simply bind to all E2 binding sites. By contrast, TBAs would distinguish the individual E2 binding sites. This is crucial as most control regions have DNA binding sites that are also contained in other non-target control regions. TBAs are unique in their ability to distinguish control regions. Thus, TBAs provide a means of creating a molecule which has high binding affinity for the target without interfering with normal cellular trafficking. Accordingly, the applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §103 based on the Frankel *et al.* reference.

Claim 49 has been rejected under 35 U.S.C. §103(a) as being unpatentable over Essigmann *et al.* (U.S. Patent No. 5,882,941). The applicants respectfully traverse this grounds for rejection.

Essigmann describes using heterobifunctional compounds where the first agent binds to cellular DNA to form a genomic lesion and the second agent is used to block DNA repair of the first agent lesion. The Office Action indicates that the Essigmann *et al.* heterobifunctional compounds act as TBAs. However, Essigmann's heterobifunctional compounds do not have the advantages of the claimed TBAs. Although a TBA may be comprised of two or more parts, the function of TBA parts, both as separate entities as well as the entire cooperatively-bound whole, are different than the parts of Essigmann's heterobifunctional-compounds. Essigmann *et al.* do not teach how to

selectively target binding regions. Therefore, the applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §103 based on the Essigmann *et al.* reference.

The applicants believe that, in view of the amendments to the claims and the above remarks, the current claims are now in condition for allowance. Such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 CFR 1.16 or 1.17 as required by this paper to Deposit Account 19-0065.

The applicants invite the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephone interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,

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Attachment: Petition and Fee for Extension of Time

Version with Markings to Show Changes Made

Claim 28:

A method of using a target binding assembly (TBA) comprising at least one nucleic acid recognition unit, and optionally one or all of the sequences selected from the group consisting of a linker sequence, an assembly sequence, an asymmetry sequence, a nuclear localization signal sequence (NLS) and an optional support attachment (OSA) wherein said TBA is administered to a patient in need of such treatment a therapeutically or prophylactically effective amount of said TBA, which comprises administering the TBA, either in the form of a purified protein complex or in the form of a recombinant vector which, upon entry into the patient is able to express the TBA, such that the TBA binds a particular double stranded nucleic acid sequence to achieve the desired prophylactic or therapeutic result.

Claim 49:

A method of assembling multimeric target binding assemblies (TBAs) *in vivo* or *in situ* which comprises introducing component TBAs into a cell, said component TBAs each [optionally] comprising a DNA recognition unit, and optionally comprising assembly sequences, asymmetry sequences, nuclear localization signal sequences, and linker sequences, such that upon proximal binding via the DNA recognition unit of each component TBA to nucleic acid sequences encountered in the nucleus or elsewhere in the cell, component [expressed] TBAs assemble into multimeric TBAs.